# Principles of Vaccination and Immunization Strategies

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## Immunology and Vaccine-Preventable Diseases

Immunology is a complicated subject, and a detailed discussion of it is beyond the scope of this text. However, an understanding of the basic function of the immune system is useful in order to understand both how vaccines work and the basis of recommendations for their use. The description that follows is simplified. Many excellent immunology textbooks are available to provide additional detail.

Immunity is the ability of the human body to tolerate the presence of material indigenous to the body ("self"), and to eliminate foreign ("nonself") material. This discriminatory ability provides protection from infectious disease, since most microbes are identified as foreign by the immune system. Immunity to a microbe is usually indicated by the presence of antibody to that organism. Immunity is generally specific to a single organism or group of closely related organisms. There are two basic mechanisms for acquiring immunity, active and passive.

Active immunity is protection that is produced by the person's own immune system. This type of immunity usually lasts for many years, often during a lifetime.

Passive immunity is protection by products produced by an animal or human and transferred to another human, usually by injection. Passive immunity often provides effective protection, but this protection wanes (disappears) with time, usually within a few weeks or months.

The immune system is a complex system of interacting cells whose primary purpose is to identify foreign ("nonself") substances referred to as antigens. Antigens can be either live (such as viruses and bacteria) or inactivated. The immune system develops a defense against the antigen. This defense is known as the immune response and usually involves the production of protein molecules by B lymphocytes, called antibodies (or immunoglobulins), and of specific cells, including T-lymphocytes (also known as cell-mediated immunity) whose purpose is to facilitate the elimination of foreign substances.

The most effective immune responses are generally produced in response to a live antigen. However, an antigen does not necessarily have to be alive, as occurs with infection with a virus or bacterium, to produce an immune response. Some proteins, such as hepatitis B surface antigen, are easily recognized by the immune system. Other material, such as polysaccharide (long chains of sugar molecules that make up the cell wall of certain bacteria) are less effective antigens, and the immune response may not provide as good protection.

### Immunity

- Self vs. nonself
- Protection from infectious disease
- Usually indicated by the presence of antibody
- Generally specific to a single organism

### Active Immunity

- Protection produced by the person's own immune system
- Often lifetime

### Passive Immunity

- Protection transferred from another animal or human
- Effective protection that wanes with time

### Antigen

- A live (e.g., viruses and bacteria) or inactivated substance capable of producing an immune response

### Antibody

- Protein molecules (immunoglobulins) produced by B lymphocytes to help eliminate an antigen

**Passive Immunity**

- Transfer of antibody produced by one human or other animal to another
- Temporary protection
- Transplacental most important source in infancy

**Sources of Passive Immunity**

- Many types of blood or blood products
- Homologous pooled human antibody (immune globulin)
- Homologous human hyperimmune globulin
- Heterologous hyperimmune serum (antitoxin)

## Passive Immunity

Passive immunity is the transfer of antibody produced by one human or other animal to another. Passive immunity provides protection against some infections, but this protection is temporary. The antibodies will degrade during a period of weeks to months, and the recipient will no longer be protected.

The most common form of passive immunity is that which an infant receives from its mother. Antibodies are transported across the placenta during the last 1–2 months of pregnancy. As a result, a full-term infant will have the same antibodies as its mother. These antibodies will protect the infant from certain diseases for up to a year. Protection is better against some diseases (e.g., measles, rubella, tetanus) than others (e.g., polio, pertussis).

Many types of blood products contain antibody. Some products (e.g., washed or reconstituted red blood cells) contain a relatively small amount of antibody, and some (e.g., intravenous immune globulin and plasma products) contain a large amount.

In addition to blood products used for transfusion (e.g., whole blood, red cells, and platelets) there are three major sources of antibody used in human medicine. These are homologous pooled human antibody, homologous human hyperimmune globulin, and heterologous hyperimmune serum.

Homologous pooled human antibody is also known as immune globulin. It is produced by combining (pooling) the IgG antibody fraction from thousands of adult donors in the United States. Because it comes from many different donors, it contains antibody to many different antigens. It is used primarily for postexposure prophylaxis for hepatitis A and measles and treatment of certain congenital immunoglobulin deficiencies.

Homologous human hyperimmune globulins are antibody products that contain high titers of specific antibody. These products are made from the donated plasma of humans with high levels of the antibody of interest. However, since hyperimmune globulins are from humans, they also contain other antibodies in lesser quantities. Hyperimmune globulins are used for postexposure prophylaxis for several diseases, including hepatitis B, rabies, tetanus, and varicella.

Heterologous hyperimmune serum is also known as antitoxin. This product is produced in animals, usually horses (equine), and contains antibodies against only one antigen. In the United States, antitoxin is available for treatment of botulism and diphtheria. A problem with this product is serum sickness, an immune reaction to the horse protein.

Immune globulin from human sources is polyclonal; it contains many different kinds of antibodies. In the 1970s, techniques were developed to isolate and "immortalize" (cause to grow indefinitely) single B cells, which led to the development of monoclonal antibody products. Monoclonal antibody is produced from a single clone of B cells, so these products contain antibody to only one antigen or closely related group of antigens. Monoclonal antibody products have many applications, including the diagnosis of certain types of cancer (colorectal, prostate, ovarian, breast), treatment of cancer (B-cell chronic lymphocytic leukemia, non-Hodgkin lymphoma), prevention of transplant rejection, and treatment of autoimmune diseases (Crohn's disease, rheumatoid arthritis) and infectious diseases.

A monoclonal antibody product is available for the prevention of respiratory syncytial virus (RSV) infection. It is called palivizumab (Synagis). Palivizumab is a humanized monoclonal antibody specific for RSV. While certain antibody products like immune globulins interfere with live-virus vaccines, monoclonal antibody products specific to one, non-vaccine microbe do not interfere with live vaccines. Since palivizumab does not contain any other antibody except RSV antibody, it will not interfere with the response to a live virus vaccine.

## Active Immunity

Active immunity is stimulation of the immune system to produce antigen-specific humoral (antibody) and cellular immunity. Unlike passive immunity, which is temporary, active immunity usually lasts for many years, often for a lifetime.

One way to acquire active immunity is to survive infection with the disease-causing form of the organism. While exceptions (like malaria) exist, in general, once persons recover from infectious diseases, they will have lifelong immunity to that disease. The persistence of protection for many years after the infection is known as immunologic memory. Following exposure of the immune system to an antigen, certain cells (memory B cells) continue to circulate in the blood (and also reside in the bone marrow) for many years. Upon reexposure to the antigen, these memory cells begin to replicate and produce antibody very rapidly to reestablish protection.

Another way to produce active immunity is by vaccination. Vaccines interact with the immune system and often produce an immune response similar to that produced by the natural infection, but they do not subject the recipient to the disease and its potential complications. Many vaccines also produce immunologic memory similar to that acquired by having the natural disease.

**Monoclonal Antibody**

- Derived from a single type, or clone, of antibody-producing cells (B cells)
- Antibody is specific to a single antigen or closely related group of antigens
- Used for diagnosis and therapy of certain cancers and autoimmune and infectious diseases, as well as prevention of transplant rejection

**Antibody for Prevention of RSV**

- Palivizumab (Synagis)
  - monoclonal
  - contains only RSV antibody
  - will not interfere with the response to a live-virus vaccine

**Active Immunity**

- Immune system produces antigen-specific humoral and cellular immunity
- Lasts for many years, often lifetime
- Sources
  - infection with disease-causing form of organism
  - vaccination

**Vaccination**

- Active immunity produced by vaccine
- Immunity and immunologic memory similar to natural infection but without risk of disease

**Classification of Vaccines**

- Live attenuated
  - viral
  - bacterial
- Inactivated

**Inactivated Vaccines**

- Whole
  - viruses
  - bacteria
- Fractional
  - protein-based
    - toxoid
    - subunit
  - polysaccharide-based
    - pure
    - conjugate

**Live Attenuated Vaccines**

- Attenuated (weakened) form of the "wild" virus or bacterium
- Must replicate to produce an immune response
- Immune response virtually identical to natural infection
- Usually produce immunity with one dose*
- Severe reactions possible
- Interference from circulating antibody
- Fragile – must be stored and handled carefully
- Viral: measles, mumps, rubella, vaccinia, varicella, zoster, yellow fever, rotavirus, intranasal influenza, oral polio**
- Bacterial: BCG**, oral typhoid

*except those administered orally
**not available in the United States

Many factors may influence the immune response to vaccination. These include the presence of maternal antibody, nature and dose of antigen, route of administration, and the presence of an adjuvant (e.g., aluminum-containing material added to improve the immunogenicity of the vaccine). Host factors such as age, nutritional factors, genetics, and coexisting disease, may also affect the response.

## Classification of Vaccines

There are two basic types of vaccines: live attenuated and inactivated. The characteristics of live and inactivated vaccines are different, and these characteristics determine how the vaccine is used.

Live attenuated vaccines are produced by modifying a disease-producing ("wild") virus or bacterium in a laboratory. The resulting vaccine organism retains the ability to replicate (grow) and produce immunity, but usually does not cause illness. The majority of live attenuated vaccines available in the United States contain live viruses. However, two live attenuated bacterial vaccines are available in the United States (Ty21a and BCG). BCG is not used as a vaccine, but as a treatment for bladder cancer.

Inactivated vaccines can be composed of either whole viruses or bacteria, or fractions of either. Fractional vaccines are either protein-based or polysaccharide-based. Protein-based vaccines include toxoids (inactivated bacterial toxin) and subunit or subvirion products. Most polysaccharide-based vaccines are composed of pure cell wall polysaccharide from bacteria. Conjugate polysaccharide vaccines contain polysaccharide that is chemically linked to a protein. This linkage makes the polysaccharide a more potent vaccine.

**General Rule: The more similar a vaccine is to the disease-causing form of the organism, the better the immune response to the vaccine**

### Live Attenuated Vaccines

Live vaccines are derived from "wild," or disease-causing, viruses or bacteria. These wild viruses or bacteria are attenuated, or weakened, in a laboratory, usually by repeated culturing. For example, the measles virus used as a vaccine today was isolated from a child with measles disease in 1954. Almost 10 years of serial passage using tissue culture media was required to transform the wild virus into attenuated vaccine virus.

To produce an immune response, live attenuated vaccines must replicate (grow) in the vaccinated person. A relatively small dose of virus or bacteria is administered, which replicates in the body and creates enough of the organism to stimulate an immune response. Anything that either damages the live organism in the vial (e.g., heat, light) or interferes with replication of the organism in the body (circulating antibody) can cause the vaccine to be ineffective.

Although live attenuated vaccines replicate, they usually do not cause disease such as may occur with the "wild" form of the organism. When a live attenuated vaccine does cause "disease," it is usually much milder than the natural disease and is referred to as an adverse reaction.

The immune response to a live attenuated vaccine is virtually identical to that produced by a natural infection. The immune system does not differentiate between an infection with a weakened vaccine virus and an infection with a wild virus. Live attenuated vaccines produce immunity in most recipients with one dose, except those administered orally. However, a small percentage of recipients do not respond to the first dose of an injected live vaccine (such as MMR or varicella) and a second dose is recommended to provide a very high level of immunity in the population.

Live attenuated vaccines may cause severe or fatal reactions as a result of uncontrolled replication (growth) of the vaccine virus. This only occurs in persons with immunodeficiency (e.g., from leukemia, treatment with certain drugs, or human immunodeficiency virus [HIV] infection).

A live attenuated vaccine virus could theoretically revert to its original pathogenic (disease-causing) form. This is known to happen only with live (oral) polio vaccine.

Active immunity from a live attenuated vaccine may not develop because of interference from circulating antibody to the vaccine virus. Antibody from any source (e.g., transplacental, transfusion) can interfere with replication of the vaccine organism and lead to poor response or no response to the vaccine (also known as vaccine failure). Live attenuated vaccines are fragile and can be damaged or destroyed by heat and light. They must be handled and stored carefully.

Currently available live attenuated viral vaccines are measles, mumps, rubella, vaccinia, varicella, zoster (which contains the same virus as varicella vaccine but in much higher amount), yellow fever, rotavirus, and influenza (intranasal). Oral polio vaccine is a live viral vaccine but is no longer available in the United States. Live attenuated bacterial vaccines are bacille Calmette-Guérin (BCG—not currently available in the US) and oral typhoid vaccine.

**Inactivated Vaccines**

- Cannot replicate
- Less affected by circulating antibody than live vaccines
- Always require multiple doses
- Immune response mostly humoral
- Antibody titer diminish with time
- May require periodic supplemental booster doses
- Whole-cell vaccines
  - viral: polio, hepatitis A, rabies, influenza*
  - bacterial: pertussis*, typhoid*, cholera*, plague*
- Fractional vaccines
- Subunits: hepatitis B, influenza, acellular pertussis, human papillomavirus, anthrax
- Toxoids: diphtheria, tetanus

*not available in the United States

## Inactivated Vaccines

Inactivated vaccines are produced by growing the bacterium or virus in culture media, then inactivating it with heat and/or chemicals (usually formalin). In the case of fractional vaccines, the organism is further treated to purify only those components to be included in the vaccine (e.g., the polysaccharide capsule of pneumococcus).

Inactivated vaccines are not alive and cannot replicate. The entire dose of antigen is administered in the injection. These vaccines cannot cause disease from infection, even in an immunodeficient person. Inactivated antigens are less affected by circulating antibody than are live agents, so they may be given when antibody is present in the blood (e.g., in infancy or following receipt of antibody-containing blood products).

Inactivated vaccines always require multiple doses. In general, the first dose does not produce protective immunity, but "primes" the immune system. A protective immune response develops after the second or third dose. In contrast to live vaccines, in which the immune response closely resembles natural infection, the immune response to an inactivated vaccine is mostly humoral. Little or no cellular immunity results. Antibody titers against inactivated antigens diminish with time. As a result, some inactivated vaccines may require periodic supplemental doses to increase, or "boost," antibody titers.

Currently available whole-cell inactivated vaccines are limited to inactivated whole viral vaccines (polio, hepatitis A, and rabies). Inactivated whole virus influenza vaccine and whole inactivated bacterial vaccines (pertussis, typhoid, cholera, and plague) are no longer available in the United States. Fractional vaccines include subunits (hepatitis B, influenza, acellular pertussis, human papillomavirus, anthrax) and toxoids (diphtheria, tetanus). A subunit vaccine for Lyme disease is no longer available in the United States.

## Polysaccharide Vaccines

Polysaccharide vaccines are a unique type of inactivated subunit vaccine composed of long chains of sugar molecules that make up the surface capsule of certain bacteria. Pure polysaccharide vaccines are available for three diseases: pneumococcal disease, meningococcal disease, and *Salmonella* Typhi. A pure polysaccharide vaccine for *Haemophilus influenzae* type b (Hib) is no longer available in the United States.

The immune response to a pure polysaccharide vaccine is typically T-cell independent, which means that these vaccines are able to stimulate B cells without the assistance of T-helper cells. T-cell–independent antigens, including poly-

saccharide vaccines, are not consistently immunogenic in children younger than 2 years of age. Young children do not respond consistently to polysaccharide antigens, probably because of immaturity of the immune system.

Repeated doses of most inactivated protein vaccines cause the antibody titer to go progressively higher, or "boost." This does not occur with polysaccharide antigens; repeat doses of polysaccharide vaccines usually do not cause a booster response. Antibody induced with polysaccharide vaccines has less functional activity than that induced by protein antigens. This is because the predominant antibody produced in response to most polysaccharide vaccines is IgM, and little IgG is produced.

In the late 1980s, it was discovered that the problems noted above could be overcome through a process called conjugation, in which the polysaccharide is chemically combined with a protein molecule. Conjugation changes the immune response from T-cell independent to T-cell dependent, leading to increased immunogenicity in infants and antibody booster response to multiple doses of vaccine.

The first conjugated polysaccharide vaccine was for Hib. A conjugate vaccine for pneumococcal disease was licensed in 2000. A meningococcal conjugate vaccine was licensed in 2005.

## Recombinant Vaccines

Vaccine antigens may also be produced by genetic engineering technology. These products are sometimes referred to as recombinant vaccines. Five genetically engineered vaccines are currently available in the United States. Hepatitis B, human papillomavirus (HPV), and influenza (one brand) vaccines are produced by insertion of a segment of the respective viral gene into the gene of a yeast cell or virus. The modified yeast cell or virus produces pure hepatitis B surface antigen, HPV capsid protein, or influenza hemagglutinin when it grows. Live typhoid vaccine (Ty21a) is *Salmonella* Typhi bacteria that have been genetically modified to not cause illness. Live attenuated influenza vaccine has been engineered to replicate effectively in the mucosa of the nasopharynx but not in the lungs.

**Polysaccharide Vaccines**

Pure polysaccharide

- pneumococcal
- meningococcal
- *Salmonella* Typhi (Vi)

Conjugate polysaccharide

- *Haemophilus influenzae* type b (Hib)
- pneumococcal
- meningococcal

**Pure Polysaccharide Vaccines**

- Not consistently immunogenic in children younger than 2 years of age
- No booster response
- Antibody with less functional activity
- Immunogenicity improved by conjugation

**Recombinant Vaccines**

- Genetic engineering technology
- Viral: hepatitis B, human papillomavirus, influenza (one brand), live attenuated influenza
- Bacterial: *Salmonella* Typhi (Ty21a)

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## The Need for Strategies to Increase Immunization Levels

An important component of an immunization provider's practice is ensuring that the vaccines reach all people who need them. While attention to appropriate administration of vaccinations is essential, it cannot be assumed that these vaccinations are being given to every person at the recommended age. Immunization levels in the United States are high, but gaps still exist, and providers can do much to maintain or increase immunization rates among patients in their practice. This chapter describes the need for increasing immunization levels and outlines strategies that providers can adopt to increase coverage in their own practice.

Vaccine-preventable disease rates in the United States are at very low levels. In 2011, only 4 cases of rubella, no cases of diphtheria, 36 cases of tetanus, and no wild-type polio were reported to CDC. Given these immunization successes, one might question the continued interest in strategies to increase immunization levels.

Resurgence of some vaccine-preventable diseases such as pertussis, expanded recommendations for influenza vaccination and HPV vaccination, and gaps in sustainable immunization efforts highlight the need to focus on immunization rates. The viruses and bacteria that cause vaccine-preventable disease and death still exist and can be passed on to unprotected persons or imported from other countries, as demonstrated by pertussis outbreaks that occurred in 2010. Diseases such as measles, mumps, or pertussis can be more severe than often assumed and can result in social and economic as well as physical costs: sick children miss school, parents lose time from work, and illness among healthcare providers can severely disrupt a healthcare system. Although levels of disease are the ultimate outcome of interest, these are a late indicator of the soundness of the immunization system. Immunization levels are a better indicator for determining if there is a problem with immunization delivery, and this chapter will focus on increasing immunization levels and the strategies healthcare providers can use to do this.

Specific concerns about U.S. immunization levels and areas for further study include the following:

Childhood immunization rates are still suboptimal. In 2011, for example, only 84.6% of children 19 to 35 months of age had received four doses of DTaP vaccine.

For other age groups, immunization rates are considerably lower than those for early childhood. According to Behavior Risk Factor Surveillance System (BRFSS) data from 2011, a

median of only 64.9% of persons 65 years of age and older received the influenza vaccine in the past 12 months, and 62.3% had ever received pneumococcal vaccine.

Rates of influenza immunization are also unacceptably low among healthcare providers, an important target population for vaccination. Typically, fewer than 70% of healthcare providers receive influenza vaccine.

Sustainable systems for vaccinating children, adolescents, and adults must be developed in the context of a changing healthcare system. High immunization rates cannot rest upon one-time or short-term efforts. Greater understanding of strategies to increase and sustain immunization levels is necessary in order to create lasting, effective immunization delivery systems.

Many strategies have been used to increase immunizations. Some, such as school entry laws, have effectively increased demand for vaccines, but the effectiveness of other strategies (e.g., advertising) is less well documented. Some proven strategies (e.g., reducing costs, linking immunization to Women Infants and Children (WIC) services, home visiting) are well suited to increasing rates among specific populations, such as persons with low access to immunization services.

One key to a successful strategy to increase immunization is matching the proposed solution to the current problem. Although a combination of strategies—directed at both providers and the public—is necessary for increasing and maintaining high immunization rates, this chapter focuses on immunization strategies for healthcare practices and providers.

## The AFIX Approach

**AFIX**

**A**ssessment

**F**eedback

**I**ncentives

e**X**change

CDC, through state and other grantees, administers a program designed to move healthcare personnel from a state of unawareness about the problem of low immunization rates in their practice to one in which they are knowledgeable, concerned, motivated to change their immunization practices, and capable of sustaining new behaviors. The acronym used for this approach is AFIX: Assessment of the immunization coverage of public and private providers, Feedback of diagnostic information to improve service delivery, Incentives to motivate providers to change immunization practices or recognition of improved or high performance, and eXchange of information among providers. First conceived by the Georgia Division of Public Health, AFIX is now being used nationwide with both public and private immunization providers and is recommended by governmental and nongovernmental vaccine programs and medical professional societies.

## Overview

The AFIX process consists of an assessment of an immunization provider's coverage rates by a trained representative from the state or other immunization grantee program, feedback of the results of the assessment to provider staff, incentives to improve deficiencies and raise immunization rates, and exchange of information and ideas among healthcare providers. Some specific characteristics of this approach have made it one of the most effective for achieving high, sustainable vaccine coverage.

**Special Characteristics of AFIX**

- Focuses on outcomes
- Focuses on providers
- Blend of advanced technology and personal interaction

First, AFIX focuses on outcomes. It starts with an assessment, producing an estimate of immunization coverage levels in a provider's office, and these data help to identify specific actions to take in order to remedy deficiencies. Outcomes are easily measurable. Second, AFIX focuses on providers, those who are key to increasing immunization rates. AFIX requires no governmental policy changes, nor does it attempt to persuade clients to be vaccinated, but instead focuses on changing healthcare provider behavior. Third, AFIX, when used successfully, is a unique blend of advanced technology and personal interaction. Much of the AFIX process can be done electronically, increasing speed and accuracy of assessment and feedback and streamlining reporting. However, the personal skills of the assessor and that person's ability to establish rapport with and motivate a provider are critical to achieving lasting results.

### Assessment

Assessment refers to the evaluation of medical records to ascertain the immunization rate for a defined group of patients, as well as to provide targeted diagnosis for improvement. This step is essential because several studies have documented that most healthcare providers, while supportive of immunizations, do not have an accurate perception of their own practice's immunization rates. Pediatricians in these studies greatly overestimated the proportion of fully immunized children in their practices. Assessment increases awareness of a provider's actual situation and provides a basis for subsequent actions by provider staff.

**Assessment**

- Evaluation of medical records to ascertain the immunization rate for a defined group
- Targeted diagnosis for improvement
- Assessment increases awareness

CDC has developed a software program, CoCASA, which enables assessment to be done electronically, is flexible enough to accommodate whatever assessment parameters are desired, and provides results that can be printed immediately. This program will be described further in the section titled "AFIX Tools and Resources".

**Feedback**

- Informing immunization providers about their performance
- Assessment with feedback creates the awareness necessary for behavior change

**How to Provide Feedback**

- With feeling and precision
- Without judgment
- With confidentiality as appropriate

## Feedback

Feedback is the process of informing immunization providers about their performance in delivering one or more vaccines to a defined client population. The work of assessment is of no use unless the results are fed back to persons who can make a change. Assessment together with feedback creates the awareness necessary for behavior change.

Feedback generally consists of the immunization program representative meeting with appropriate provider staff and discussing the results of the assessment in order to determine the next steps to be taken. This may be done at a second visit following the assessment of the provider's records, or it may take place the same day. There are advantages and disadvantages to each approach. If CoCASA has been used, the summary report that is generated can identify specific subsets of patients (e.g., those who have not completed the series because of a missed opportunity for immunization) that, if found in substantial numbers, can provide clues to which changes in the provider's practice would be most effective. This can save time and make the feedback session more focused.

The personal element of feedback, as mentioned, is also critical to its success. A reviewer who is involved and committed to the AFIX process, who addresses deficiencies without judgment, and who respects the confidentiality of the data and the efforts of the provider, will be likely to gain the trust of providers and motivate them to increase immunization rates in the practice.

**Incentives**

- Something that incites to action or effort
- Vary by provider and stage of progress
- Opportunities for partnership and collaboration

## Incentives

An incentive is defined as something that incites one to action or effort. Incentives are built into the AFIX process, recognizing that immunization providers, like everyone else, will accomplish a desired task more successfully if motivated to do so. The assessment and feedback components are not intended to be done in isolation; providers may have sufficient data about their practice's immunization rates, but they must recognize high immunization coverage as a desirable goal and be motivated to achieve it.

Incentives are extremely variable. No one thing will be effective for every provider, and a single provider may need different types of motivation at different stages of progress. Things like small tokens of appreciation and providing resource materials at meetings have helped providers approach their task positively and create an atmosphere of teamwork, but longer-term goals must be considered as well. Since the effort to raise immunization rates may involve an increase in duties for staff, offering assistance in reviewing records or sending reminder notices might

more directly address a provider's needs. Incentives pose a challenge to the creativity of the program representative but also offer the opportunity to try new ideas.

Finally, incentives are opportunities for partnerships and collaboration. Professional organizations or businesses have been solicited to publicize the immunization efforts in a newsletter or provide funding for other rewards for provider staff. Many other types of collaboration are possible; these also have the benefit of increasing awareness of immunization among diverse groups.

### eXchange of Information

The final AFIX component, eXchange of information, goes hand in hand with incentives. The more information providers have about their own practice's immunization coverage status, how it compares with state norms and with other providers in their community, and what strategies have been successful with other providers, the more knowledgeable and motivated they will be to increase their immunization rates. It is up to the AFIX representative to provide appropriate statistical and educational information and create forums for exchange of information among providers.

**eXchange of Information**

- Allows access to more experience than an individual can accumulate
- Motivates improvement
- Coordinates resources and efforts

Staff members at all levels can benefit from the exchange of ideas about immunization practices and increasing rates of coverage—what has worked or not worked with another provider, streamlining office procedures, or where to obtain educational or other resources. The forums for such exchanges vary widely from informal meetings on the local level to more structured meetings sponsored by government or professional organizations. Immunization training sessions can be combined with sharing of ideas regarding actual situations in which recommendations, such as those from ACIP, are applied.

With the increased use of electronic communication, this method should not be neglected in the information exchange component of AFIX. Although different from face-to-face communication, e-mail exchanges or newsletters sent electronically can be cost-saving and fast means of disseminating information.

## VFC/AFIX Initiative

Responsibility for immunization has largely shifted from public health departments to private providers, who now vaccinate nearly 80% of children in the United States. Many of these providers participate in the Vaccines for Children (VFC) program, a federal program whereby funding is provided for state and other immunization programs to purchase vaccines and make them available at no cost to children who meet income eligibility requirements. CDC launched an initiative in 2000 to link some AFIX and VFC

**VFC/AFIX**

- 2000: Incorporate AFIX activities during VFC site visits
- 2013: VFC visits performed separately from AFIX visits
- VFC/AFIX visits may be combined if state has robust IIS, which assists with AFIX component

activities and incorporate AFIX activities during VFC provider site visits in an attempt to avoid duplication of staff time and effort. However, reported concerns with proper storage and handling of vaccine led the federal VFC program to revise this approach. Beginning in 2013, VFC program staff are encouraged to perform VFC compliance visits separate from the AFIX visit to focus on the core components of each program, including the assessment of, and provider training related to, proper vaccine storage practices. VFC programs may choose to continue to combine these program efforts if the state has a robust Immunization Information System (IIS) that assists with performing the AFIX assessment portion of the visits.

VFC serves more than 40,000 private provider sites, and every state participates in the program. VFC provider site visits are conducted to review compliance with federal program requirements, including VFC eligibility screening, and to evaluate vaccine storage and handling procedures. Information about VFC can be found at http://www.cdc.gov/vaccines/programs/vfc/default.htm.

## AFIX Tools and Resources

CDC has developed a software program titled Comprehensive Clinic Assessment Software Application (CoCASA) to enable electronic entry of AFIX and VFC site visit data. CoCASA, first released in December 2005, is an update of previous versions of CASA and supersedes previous versions. Using CoCASA, a reviewer enters appropriate basic information about an individual provider and conducts an assessment of patient records. The user also has the option to record AFIX visit outcomes and VFC site visit information.

**Comprehensive Clinic Assessment Software Application (CoCASA)**

- VFC and AFIX results
- Immediate assessment results
- Estimate of coverage levels
- Reasons for deficiencies
- Reports on patient subsets

**AFIX Guide to the Core Elements for Training and Implementation**

- Generalizes the AFIX process
- Provides strategies for modifying AFIX methodology

CoCASA can provide immediate results of the assessment, supplying the reviewer with the information needed for use in the feedback session and noting areas that need further follow-up. CoCASA saves the reviewer time and provides various analysis options. CoCASA reports provide estimates of immunization coverage levels and potential reasons for the coverage level, such as missed opportunities for immunization and patients who did not return to finish the immunization series. The program can generate reports on specific sets of patients. Data from an immunization registry or patient management system can be imported into CoCASA, and data collected during the visit can be exported for further analysis.

Additional resources available for AFIX include the AFIX Guide to the Core Elements for Training and Implementation document. This document generalizes the AFIX process so that it can be applied to any age group and when differences between populations do exist with respect

to the AFIX process, this document clearly identifies the difference and provides helpful strategies for modifying the AFIX methodology.

CoCASA is available on the CDC Vaccines and Immunization website at http://www.cdc.gov/vaccines/programs/cocasa/index.html. Additional information about AFIX, including the Core Elements document, is available on the CDC Vaccines and Immunization website at http://www.cdc.gov/vaccines/programs/afix/index.html.

### AFIX Endorsements

AFIX is widely supported as an effective strategy to improve vaccination rates. Many states have shown gradual and consistent improvement in their coverage levels in the public sector, and studies of private pediatricians have also documented substantial improvements in median up-to-date coverage at 24 months. Assessment and feedback of public and private provider sites are recommended by the National Vaccine Advisory Committee (NVAC) in the Standards of Pediatric Immunization Practices, as well as by the Advisory Committee on Immunization Practices (ACIP) in a statement endorsing the AFIX process and recommending its use by all public and private providers. Furthermore, Healthy People 2020 has an objective to increase the proportion of immunization providers who have measured vaccination levels among children in their practice within the past year.

One of the Standards for Adult Immunization Practices issued by NVAC calls upon providers of adult immunization to do annual assessments of coverage levels. Although the use of AFIX among providers who serve adults is not as widespread as among childhood immunization providers, this strategy can be a powerful tool to improve rates in the adult population.

## Other Essential Strategies

Although a substantial portion of this chapter is devoted to AFIX, certain other strategies for improvement of immunization levels deserve emphasis. These are complementary to AFIX; their adoption will support the goals of AFIX, i.e., raising immunization coverage levels, and will facilitate the AFIX process and ensure a favorable outcome of an assessment.

### Recordkeeping

Patient records are of vital importance in a medical practice, and maintaining these records, whether paper or electronic, is critical to providing optimal healthcare. Immunization records, specifically, should meet all applicable legal requirements as well as requirements of any specific program, such as VFC, in which the provider participates. These

**Strategies for High Immunization Levels**

- Recordkeeping
- Immunization Information Systems (IIS)
- Recommendations and reinforcement
- Reminder and recall to patients
- Reminder and recall to providers
- Reduction of missed opportunities
- Reduction of barriers to immunization

**Records**

- Available for inspection
- Easy to interpret
- Accurate, up-to-date, and complete
  - reflect current patient population
  - reflect all vaccines given

records should be available for inspection by an AFIX or VFC representative and should be easy to interpret by anyone examining the record.

Immunization records must be accurate. The active medical records must reflect which patients are actually in the practice; charts of persons who have moved or are obtaining services elsewhere should be clearly marked accordingly or removed. Records should be kept up-to-date as new immunizations are administered, and all information regarding the vaccine and its administration should be complete.

Because patients often receive vaccines at more than one provider office, communication between sites is necessary for maintaining complete and accurate immunization records. School-based, public health, and community-based immunization sites should communicate with primary care personnel through quick and reliable methods such as immunization information systems, telephone, fax, or e-mail. This will become increasingly important as venues outside the medical home offer immunizations.

## Immunization Information Systems (IIS)

**Immunization Information Systems (IIS)**

- Single data source for all providers
- Reliable immunization history
- Produce records for patient use
- Increase vaccination rates

Many recordkeeping tasks, as well as patient reminder/recall activities, can be greatly simplified by participation in a population-based immunization information system (IIS), also known as an immunization registry. An IIS is a computerized information system that contains information about the immunization status of each child in a given geographic area (e.g., a state). In some areas, an IIS is linked to a child's complete medical record. An IIS provides a single data source for all community immunization providers, enabling access to records of children receiving vaccinations at multiple providers. It provides a reliable immunization history for every enrolled child and can also produce accurate immunization records if needed for school or summer camp entry.

The Task Force on Community Preventive Services recommends immunization information systems on the basis of strong evidence of effectiveness in increasing vaccination rates. Specifically, the Task Force concluded that IIS are directly related to increasing vaccination rates through their capabilities to create or support effective interventions such as client reminder/recall systems, provider assessment and feedback, and provider reminders; generate and evaluate public health responses to outbreaks of vaccine-preventable disease; facilitate vaccine management and accountability; determine client vaccination status for decisions made by clinicians, health departments, and schools; and aid surveillance and investigations on vaccination rates, missed vaccination opportunities, invalid dose administration, and disparities in vaccination coverage.

A goal of *Healthy People 2020* is to increase to 95% the proportion of children younger than 6 years of age who participate in fully operational, population-based immunization registries. In 2011, approximately 84% of children in this age group met this participation goal. Federal, state, and local public health agencies are continuing their efforts to improve the registries themselves and to increase participation by immunization providers. IIS are a key to increasing and maintaining immunization levels and provide benefits for providers, patients, and state and federal immunization program personnel. More information about IIS is available on the CDC Vaccines and Immunization website at http://www.cdc.gov/vaccines/programs/iis/index.html.

## Recommendations to Parents and Reinforcement of the Need to Return

The recommendation of a healthcare provider is a powerful motivator for patients to comply with vaccination recommendations. Parents of pediatric patients are likely to follow vaccine recommendations of the child's doctor, and even adults who were initially reluctant were likely to receive an influenza vaccination when the healthcare provider's opinion of the vaccine was positive.

Regardless of their child's true immunization status, many parents believe the child is fully vaccinated. Parents may not have been told or may not have understood that return visits are necessary. It is useful for patients to have the next appointment date in hand at the time they leave the provider's office. An additional reminder strategy is to link the timing of the return visit to some calendar event, (e.g., the child's birthday or an upcoming holiday). Even with written schedules or reminders, a verbal encouragement and reminder can be an incentive for a patient's completing the immunization series and can ultimately result in higher coverage levels.

## Reminder and Recall Messages to Patients

Patient reminders and recall messages are messages to patients or their parents stating that recommended immunizations are due soon (reminders) or past due (recall messages). The messages vary in their level of personalization and specificity, the mode of communication, (e.g., postcard, letter, telephone), and the degree of automation. Both reminders and recall messages have been found to be effective in increasing attendance at clinics and improving vaccination rates in various settings.

Cost is sometimes thought to be a barrier to the implementation of a reminder/recall system. However, a range of options is available, from computer-generated telephone calls and letters to a card file box with weekly dividers, and

**Recommendations and Reinforcement**

- Recommend the vaccine
  - powerful motivator
  - patients likely to follow recommendation of the provider
- Reinforce the need to return
  - verbal
  - written
  - link to calendar event

**Reminders and Recall to Patients**

- Reminder—notification that immunizations are due soon
- Recall—notification that immunizations are past due
- Content of message and technique of delivery vary
- Reminders and recall have been found to be effective

**Reminders and Recall to Providers**

- Communication to healthcare providers that a patient's immunizations are due soon or past due
- Examples
  - computer-generated list
  - stamped note in the chart
  - "Immunization Due" clip on chart
  - electronic reminder in an electronic medical record

these can be adapted to the needs of the provider. The specific type of system is not directly related to its effectiveness, and the benefits of having any system can extend beyond immunizations to other preventive services and increase the use of other recommended screenings.

Both the Standards for Child and Adolescent Immunization Practices and the Standards for Adult Immunization Practices call upon providers to develop and implement aggressive tracking systems that will both remind parents of upcoming immunizations and recall children who are overdue. ACIP supports the use of reminder/recall systems by all providers. The National Center for Immunization and Respiratory Diseases provides state and local health departments with ongoing technical support to assist them in implementing reminder and recall systems in public and private provider sites.

## Reminder and Recall Messages to Providers

Providers can create reminder and recall systems that help them remember which patients' routine immunizations are due soon or past due. Provider reminder/recall is different from "feedback," in which the provider receives a message about overall immunization levels for a group of clients. Examples of reminder/recall messages are:

- A computer-generated list that notifies a provider of the children to be seen that clinic session whose vaccinations are past due.
- A stamp with a message such as "No Pneumococcal Vaccine on Record," that a receptionist or nurse can put on the chart of a person age 65 years or older.
- An "Immunization Due" clip that a nurse attaches to the chart of an adolescent who has not had HPV vaccine.
- An electronic reminder which appears when providers access an electronic medical record.

Reminder systems will vary according to the needs of the provider; in addition to raising immunization rates in the practice, they will serve to heighten the awareness of staff members of the continual need to check the immunization status of their patients.

**Missed Opportunity**

A healthcare encounter in which a person is eligible to receive vaccination but is not vaccinated completely

## Reduction of Missed Opportunities to Vaccinate

A missed opportunity is a healthcare encounter in which a person is eligible to receive a vaccination but is not vaccinated completely. Missed opportunities occur in all settings in which immunizations are offered, whether routinely or not.

Missed opportunities occur for several reasons. At the provider level, many nurses and physicians avoid simultaneous administration of four or even three injectable vaccines. Frequently stated reasons have included concern about reduced immune response or adverse events, and parental objection. These concerns are not supported by scientific data. Providers also may be unaware that a child (or adult) is in need of vaccination (especially if the immunization record is not available at the visit) or may follow invalid contraindications (see Chapter 2 for more information).

**Reasons for Missed Opportunities**

- Lack of simultaneous administration
- Unaware child (or adult) needs additional vaccines
- Invalid contraindications
- Inappropriate clinic policies
- Reimbursement deficiencies

Some of the reasons for missed opportunities relate to larger systems; (e.g., a clinic that has a policy of not vaccinating at any visits except well-child care, or not vaccinating siblings). Other reasons relate to large institutional or bureaucratic regulations, such as state insurance laws that deny reimbursement if a vaccine is given during an acute-care visit. The degree of difficulty in eliminating the missed opportunity may vary directly with the size of the system that has to be changed.

Several studies have shown that eliminating missed opportunities could increase vaccination coverage by up to 20 percent. Strategies designed to prevent missed opportunities have taken many different forms, used alone or in combination. Examples include the following:

- **Standing orders.** These are protocols whereby nonphysician immunization personnel may vaccinate clients without direct physician involvement at the time of the immunization. Standing orders are implemented in settings such as clinics, hospitals, and nursing homes. When used alone or in combination with other interventions, standing orders have had positive effects on immunization rates among adults and children.

- **Provider education.** Anyone responsible for administering immunizations should be knowledgeable about principles of vaccination and vaccination scheduling, to the extent required for their position. Providers are largely responsible for educating their patients, so an investment in provider education will result in a higher level of understanding about immunizations among the public in general. Numerous educational materials, in a variety of formats, are available from CDC, the Immunization Action Coalition, and some state health departments, hospitals, or professional organizations. Incorporating some AFIX principles (i.e., assessment, feedback) into a provider education program might have a greater effect on provider behavior than an education effort aimed only at increasing knowledge.

**Strategies for Reducing Missed Opportunities**

- Standing orders
- Provider education with feedback
- Provider reminder and recall systems

- **Provider reminder and recall systems.** Provider reminder and recall systems are discussed earlier in the chapter. These reminder systems, while effective in increasing immunization levels, can also help avoid missed opportunities if they are a component of other practices directed toward this goal. For example, if a reminder system is used consistently and staff members are knowledgeable about vaccination opportunities and valid contraindications, the system can be an additional aid in promoting appropriate immunization practices.

## Reduction of Barriers to Immunization Within the Practice

**Reduction of Barriers to Immunization**

- Physical barriers
  - clinic hours
  - waiting time
  - distance
  - cost
- Psychological barriers
  - unpleasant experience
  - vaccine safety concerns

Despite efforts by providers to adhere to appropriate immunization practices, obstacles to vaccination of patients may exist within the practice setting, sometimes unknown to the provider. Barriers to immunization may be physical or psychological. Physical barriers might be such things as inconvenient clinic hours for working patients or parents, long waits at the clinic, or the distance patients must travel. Providers should be encouraged to determine the needs of their specific patient population and take steps, such as extending clinic hours or providing some immunization clinics, to address obstacles to immunization.

Cost is also a barrier to immunization for many patients. In addition to evaluating their fee schedule for possible adjustments, providers should be knowledgeable about such programs as Vaccines for Children and the State Children's Health Insurance Program and the provisions specific to their state. Enrollment as a VFC provider is recommended for those with eligible children in their practice.

Psychological barriers to healthcare are often more subtle but may be just as important. Unpleasant experiences (e.g., fear of immunizations, being criticized for previously missed appointments, or difficulty leaving work for a clinic appointment) may lead clients to postpone receiving needed vaccinations. Concerns about vaccine safety are also preventing some parents from having their children immunized. Overcoming such barriers calls for both knowledge and interpersonal skills on the part of the provider—knowledge of vaccines and updated recommendations and of reliable sources to direct patients to find accurate information, and skills to deal with fears and misconceptions and to provide a supportive and encouraging environment for patients. For more information on provider resources, see http://www.cdc.gov/vaccines/hcp/patient-ed/conversations/.

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